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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1616	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/531,867	CHURCH ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☒ Claim(s) *5-8,10,12-17 and 19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/20/06; 2/28/06; 4/19/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are pending.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

Claims 5-8, 10, and 12-17 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only, and/or cannot depend from any other multiple dependent claim. See MPEP § 608.01(n).

Claim 19 is objected to because of the following informalities: the word "chronic" is improperly capitalized, because it is not a proper noun. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 10-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement regarding the recitation of salmeterol solvates. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Determination of Claim Scope

Claim 1 of the instant application claims a solution aerosol pharmaceutical composition comprising (i) no more than 35% w/w co-solvent, (ii) a liquefied HFA propellant, (iii) 0-5 % w/w water, and (iv) an active agent selected from salmeterol or a stereoisomer, physiologically acceptable salt, and solvate thereof.

Review of Applicants' Disclosure

The instant specification does not disclose, to which solvates of salmeterol Applicants are referring. Applicants' specification does not disclose how to make any particular solvate of salmeterol, nor do Applicants depict chemical structures of salmeterol as any particular solvate in their disclosure.

Possession Based on Ordinary Skilled Artisan's Determination/ State of the Prior Art

It is generally accepted in the art that the formation of a particular solvate, polymorph, or hydrate for a given compound or series of compounds is unpredictable (see Vippagunta et al. "Crystalline Solids," *Advanced Drug Delivery Reviews*, **2001**, *48*, 1-26, especially pp 1, 11-12, and 18),therefore, the generic reference to a solvate of either [specify species] in the instant specification does not provide adequate written support for claims drawn to any solvate or hydrate of these compounds. Braga et al. (*Chem. Commun.*, "Making Crystals from Crystals: a green route to crystal engineering and polymorphism," **2005**, pp 3635-3645) states on page 3640, "One can say that if the formation of polymorphs is a nuisance for crystal engineers, solvate formation can be a nightmare, because it is extremely difficult to predict whether a new species may crystallize[s] from solution with one or more molecules of solvent." A search of the prior art did not uncover any reports of the preparation of any specific salmeterol solvate.

An ordinary skilled artisan would conclude that Applicants were not in possession of the genus of salmeterol solvates, compositions comprising said solvates, or methods of making said compositions comprising said solvates. Furthermore, because Applicants' generic reference to solvates of salmeterol does not permit the ordinary skilled artisan to clearly envisage which specific solvates were in Applicants' possession, the only reasonable conclusion said artisan would make was that Applicants were not in possession of any solvates of salmeterol and had not reduced to practice the preparation, isolation, and characterization of said solvates.

The remaining claims are rejected as depending from a rejected claim.

Claims 1-7 and 10-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) compositions comprising salmeterol or

stereoisomers and physiologically acceptable salts thereof and (ii) processes of making the compositions of (i), does not reasonably provide enablement for compositions comprising solvates of salmeterol or methods of making compositions comprising solvates of salmeterol. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

An analysis based upon the Wands factors is set forth below.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993),. See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman (230 USPQ 546, 547 (Bd Pat App Int 1986)). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Breadth of Claims

Applicants' claims are broad with regards to the subgenera of solvates, stereoisomers, and physiologically acceptable salts of salmeterol.

Nature of the invention/State of the Prior Art

Claim 1 of the instant application claims a solution aerosol pharmaceutical composition comprising (i) no more than 35% w/w co-solvent, (ii) a liquefied HFA propellant, (iii) 0-5 % w/w water, and (iv) an active agent selected from salmeterol or a stereoisomer, physiologically acceptable salt, and solvate thereof. It is generally accepted in the art that the formation of a particular solvate or hydrate for a given compound or series of compounds is unpredictable (see Vippagunta et al. "Crystalline Solids," *Advanced Drug Delivery Reviews*, **2001**, *48*, pp 11 and 18). Braga et al. (*Chem. Commun*., "Making Crystals from Crystals: a green route to crystal engineering and polymorphism," **2005**, pp 3635-3645) states on page 3640, "One can say that if the formation of polymorphs is a nuisance for crystal engineers, solvate formation can be a nightmare, because it is extremely difficult to predict whether a new species may crystallize[s] from solution with one or more molecules of solvent." The prior art does not teach or identify any specific solvate of salmeterol or methods of making any specific solvate of salmeterol.

Level of One of Ordinary Skill & Predictability/Unpredictability in the Art

The level of a person of ordinary skill in the art is high, with ordinary artisans having advanced medical and/or scientific degrees (e.g. M.D., Ph.D., Pharm. D. or combinations thereof). There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427, F. 2d 833, 166, USPQ 18 (CCPA 1970). The art is especially unpredictable with regards to the existence and formation of particular polymorphs and pseudopolymorphs (e.g. hydrates and solvates) of chemical compounds, as set forth above by the teachings of Vippagunta et al. and Braga.

Guidance/Working Examples

Applicants provide no guidance or working examples about the preparation of any solvate of salmeterol.

In conclusion, the specification, while being enabling for (i) compositions comprising salmeterol or stereoisomer and physiologically acceptable salts thereof and (ii) methods of making the compositions of (i), does not reasonably provide enablement for compositions comprising solvates of salmeterol or methods of making compositions comprising salmeterol solvates.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is vague and indefinite, because an ordinary skilled artisan would not have been able to ascertain the metes and bounds of a (poly)alkoxy derivative. The 10th edition of the Merriam-Webster's Collegiate Dictionary (Merriam-Webster Incorporated: Springfield, Massachusetts, 1993, pp 311) defines "derivative" as, "a chemical substance related structurally to another substance and theoretically derivable from it." For example, carbon dioxide water could theoretically be derived from the combustion of a (poly)alkoxy derivative compound. Therefore, the definition of derivative in the Merriam-Webster Collegiate Dictionary does not shed light on what Applicants' intended for the meaning of a (poly)alkoxy derivative.

Regarding claims 15 and 20, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 6 is indefinite, because to understand what is being claimed one must refer to page 16, lines 16-24 of the specification. This is improper. Appropriate correction is required.

The remaining claims are rejected as depending from a rejected claim.

Claim Rejections - 35 USC § 102

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 5-9, 12-13, and 18-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Cripps et al. (US 2005/0048001).

Applicants claim a pharmaceutical aerosol formulation comprising (a) dissolved salmeterol, (ii) a liquefied HFA propellant system, (iii) co-solvent in an amount of no more than 35% w/w, and (iv) water in an amount of 0-5% w/w.

Cripps exemplifies a formulation comprising **0.05% w/w salmeterol xinafoate, 30% w/w ethanol, 1.3% w/w glycerol, and remainder 1,1,1,2-tetrafluoroethane** ([0072]-[0073]). Cripps discloses a methods of making a pharmaceutical aerosol solution formulations, wherein in one embodiment the method comprises **(i) dissolution of medicament (e.g. salmeterol) in the solubilizing agent (e.g. ethanol) with any low-volatility component (e.g. glycerol or PEG), (ii) transfer of the solution into an empty canister, (iii) crimping of a metering valve onto the canister, and (iv) filling propellant into the canister via the valve** ([0056]-[0058]). Cripps

discloses that the formulations may contain, in addition to salmeterol, **additional medicaments, such as corticosteroids or anti-cholinergic compounds** [0049].

Cripps discloses that ethanolic/HFA solutions of salmeterol may undergo chemical degradation due to acid-catalyzed dimerization of salmeterol or oxidation. **Dimerization may be minimized by the inclusion of** a small amount of a base (e.g. amine or carbonate) and/or a **small amount of water (e.g. 0.05-2% w/w)** [0050].

Cripps discloses that depending upon the final concentration of salmeterol or a salt thereof the concentration of ethanol required will vary. The amount of ethanol should not exceed 40% w/w, preferably it does not exceed 35% w/w. **The amount of ethanol is preferably 5-30% w/w (e.g. 13-24% w/w) and the amount of salmeterol xinafoate is typically in the range of 0.02-0.05% w/v [0044]**.

Cripps teaches that the **aluminum canisters/inhalers used to store the invented formulations may be anodized or coated with an inert polymer such as a blend of polyethersulphone (PES) and polytetrafluoroethane (PTFE) or alternatively a coating of poly (fluorinated ethylene propylene) (FEP)**.

Cripps discloses that **it is advantageous for the actuator orifice diameter to be 0.25 mm or less, preferably 0.22 mm** [0061].

Concerning the properties recited in claims 6-7 of the instant application, because the formulations disclosed by Cripps are the same as those claimed both formulations must exhibit the same properties.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-9, 12-13, 15, and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Cripps (WO 01/47493) (Cripps-WO).

Applicants claim a pharmaceutical formulation as described above, wherein in some embodiments the formulation comprises additional active agents, such as steroids.

Cripps discloses on pages 14-16:

> Examples 1 and 2
>
> Formulations may be prepared with composition as follows:
>
> Salmeterol xinafoate: 0.025% w/v
>
> Fluticasone propionate: 0.05% w/v
>
> Ethanol: 22% w/w
>
> Glycerol: 1.3% w/w
>
> 1,1,1,2-tetrafluoroethane: to 100%
>
> This solution formulation may be filled into an aluminium canister under pressure and fitted with a metering valve having a 100 µl metering chamber.

> Examples 6-8
>
> Formulations were prepared with composition as follows:
>
> Salmeterol (as free base): 0.025% w/v
>
> Fluticasone propionate: 0.025% w/v
>
> Ethanol: 7% w/w
>
> Glycerol or PEG200 or PEG400: 0.5% w/w
>
> 1,1,1,2-tetrafluoroethane: to 100%
>
> These solution formulations were filled into an aluminium canister (120 actuations/canister; overage of 40 actuations) under pressure and fitted with a metering valve (Valois DF60) having metering chamber of volume 100 µl. These formulations are suitable for delivering 25 µg salmeterol and 25 µg fluticasone propionate per actuation.

Andersen Cascade Impaction Data

Formulations as described in Examples 6 to 11 were profiled using an Andersen Cascade Impactor, using a 0.22mm (orifice) x 0.65mm (jet length) actuator from Bespak (BK621 variant). Testing was performed on canisters at "beginning of use" (BoU) and

Cripps discloses that ethanolic/HFA solutions of salmeterol may undergo chemical degradation due to acid-catalyzed dimerization of salmeterol or oxidation. **Dimerization may be minimized by the inclusion of** a small amount of a base (e.g. amine or carbonate) and/or a **small amount of water (e.g. 0.05-2% w/w)** (pg. 10, lines 21-30).

Cripps discloses that **it is advantageous for the actuator orifice diameter to be 0.25 mm or less, preferably 0.22 mm** (pg. 12, line 29 through pg. 13, line 2).

Concerning the properties recited in claims 6-7 of the instant application, because the formulations disclosed by Cripps are the same as those claimed both formulations must exhibit the same properties.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims

2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cripps (WO 01/47493) (Cripps-WO) or alternatively Cripps et al. (US 2005/0048001).

Applicant Claims

Applicants' claim a formulation as described above wherein in some embodiments (1) the formulations comprises water and ethanol in amounts of 0.5-5% w/w (water) and no more than 25% w/w; or (2) the formulation comprises 0.04% w/v salmeterol, 15% w/w ethanol, and 2% w/w water. Applicants also claim a method of formulating a pharmaceutical aerosol formulation comprising (i) preparing a solution of one or more medicaments in one or more solvents, (ii) optionally adding a proper amount of water and adjusting the pH of the solution, (iii) filling the device with the solution, (iv) crimping with valves and gassing, and (v) adding HFA propellant.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Cripps and Cripps-WO have been set forth above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Cripps and Cripps-WO lack the exemplification of compositions as described above in the instant rejection and a method of preparing a pharmaceutical aerosol formulation as described above in the instant rejection. These deficiencies are rendered obvious per the teachings of Cripps and Cripps-WO.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie to obtain pharmaceutical aerosol solution formulations of salmeterol containing water in amounts of 0.5-5% w/w, because Cripps teaches that overlapping amounts of water (i.e. 0.05%-2% w/w) are sometimes necessary to prevent the undesirable dimerization (i.e. degradation) of salmeterol. An ordinary skilled artisan would have been motivated to add water in the amounts taught by Cripps to prevent salmeterol from degrading upon storage. An ordinary skilled artisan would have had a reasonable expectation of successfully formulating said formulations with water, because Cripps explicitly suggests the addition of water in overlapping amounts. Regarding the specific amounts of salmeterol and ethanol, Cripps also teaches overlapping ranges for these two components. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine

practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Concerning the claimed method, it is noted that step (iii), in which acid is added is an optional. Regarding the remaining steps, crimping and gassing, these steps are explicitly identified by Cripps. Thus, it would have been prima facie obvious to prepare the formulations invented by Cripps utilizing the method taught by Cripps and obtain the claimed formulations of the instant application, because Cripps formulations are identical to most of the formulations claimed by Applicants. An ordinary skilled artisan would have had a reasonable expectation of successfully preparing Applicants' claimed formulations by following Cripps instructions, because Cripps formulations are the same or substantially similar to those claimed by Applicants. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference

claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 6-7, 12-14, and 18-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-10 of U.S. Patent No. 7,347,199 (USPN '199). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims claim formulations or pressurized metered dose inhalers (pMDIs) containing formulations comprising dissolved salmeterol, a hydrofluorocarbon propellant (e.g. HFA 227, HFA 134a, or mixtures thereof), cosolvent (e.g. ethanol or polyethylene glycol). The primary difference between the claims of the instant application and the claims of USPN '199 is that the claims of USPN '199 do not recite the limitation that the compositions contain water in an amount of 0-5% w/w. This deficiency is prima facie obvious, because the claims of USPN '199 do not indicate that water has been added. Thus, the claims of USPN '199 necessarily comprise 0% w/w water and are an obvious variant of the claims of the instant application. It is noted that claim 10 of USPN '199 claims a pMDI wherein the active agent is a beta-adrenergic agonist selected from the group consisting of salbutamol, formoterol, salmeterol, and TA 2005, wherein the pMDI also contains in solution (i) propellant selected from HFA 227, HFA 134a, or mixtures thereof, (ii) ethanol as the co-solvent,

and (iii) a low volatility component including glycerol, polyethylene glycol, etc. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-3, 6-7, 12-14, and 18-21 *prima facie* obvious over claims 7-10 of U.S. Patent No. 7,347,199 (USPN '199).

(1) Claims 1-3, 5-7, 9-12, and 14-17 are provisionally rejected as being unpatentable over claims 2-3, 6-7, 11, 19, 22, 24, 28-32, 35-36, 40-47, 50-52 of copending Application No. 10/504,151 (copending '151) in view of Lewis et al. (U.S. Patent No. 6,716,414) ("Lewis"); (2) claims 1-7, 9-12, and 14-17 are provisionally rejected as being unpatentable over claims 1, 3-18, 20-42, and 44-45 of copending Application No. 10/505,861 (copending '861); and (3) claims 1-3, 5, and 10 are provisionally rejected as being unpatentable over claims 14-15 and 25-26 of copending Application No. 11/408,026 (copending '026).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are overlapping in scope and mutually obvious. Independent claim 1 of the instant application claims a pharmaceutical aerosol solution formulation comprising salmeterol active agent, HFA propellant, cosolvent, 0-5% w/w water (0% water reads on less than 500-1,500 ppm water), wherein the amount of cosolvent is no more than 35% w/w of the total weight of the formulation. Independent claim 32 of copending '151 claims a standard aluminum container containing a pharmaceutical aerosol solution formulation comprising (1) an active agent selected from formoterol or a stereoisomer, physiologically acceptable salt, and solvate thereof, (2) a liquefied HFA propellant, (3) a co-solvent, and (4) less than 1,500 ppm of water based on the total weight of the formulation. The cited dependent

claims of the instant application and of copending '151 have similar and overlapping co-solvent Markush groups, claimed particle sizes, pH ranges, additional active agent Markush groups, and the same steps in the claimed methods of preparing pharmaceutical formulations. The other cited dependent claims in both applications also recite the same or substantially similar limitations.

The primary difference between applications is that the claims of copending '151 require that the principal active agent is formoterol and excluding claim 14 of copending '151, the claims of the instant application do not specify the container material. This deficiency is cured in part by the teachings of Lewis, which is solely provided to demonstrate that salmeterol, formoterol, and TA 2005 are art recognized as being beta2-agonist bronchodilators (col. 5, lines 30-33 of Lewis), and those are all expected to exhibit similar bronchodilating effects. Regarding the use of a standard aluminum canister, this would have been prima facie obvious modification, as evidenced by claim 13 of the instant application, which explicitly identifies standard aluminum as a suitable canister material. Therefore, it would have been obvious to substitute one beta2 agonist for another, to use standard aluminum as the canister material, and an ordinary skilled artisan would have had a reasonable expectation that upon substitution the resulting formulation would have similar bronchodilating properties. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-3, 5-7, 9-12, and 14-17 *prima facie* obvious over claims 2-3, 6-7, 11, 19, 22, 24, 28-32, 35-36, 40-47, 50-52of copending Application No. 10/504,151 (copending '867) in view of Lewis et al. (U.S. Patent No. 6,716,414) ("Lewis"). Similar reasoning was used in the analysis of copending '861 and copending 11/408,026.

This is a provisional obviousness-type double patenting rejection.

Claims 1-3, 5, 15, and 18-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6-11, and 13 of copending Application No. 12/225,075 (copending '075). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending '075 claim a method for the treatment of respiratory diseases (e.g. COPD or asthma) requiring the administration of a substantially similar pharmaceutical aerosol solution formulation as claimed in the instant application intended for the treatment of respiratory diseases (e.g. asthma or COPD). Independent claim 1 of copending '075 claims a method for the prevention and/or treatment of sever broncho-pulmonary disease comprising administering a solution formulation comprising two or more dissolved active agents in an HFA propellant and a co-solvent. Dependent claim 3 of copending '075 limits parent claim 1 to comprise at least one member of the group consisting of formoterol, carmoterol, indacaterol, salmeterol, and stereoisomers, salts, solvates, or salt solvates thereof. Dependent claims 6-11 of copending '075 further limit parent claim 1 to specify that the formulation comprises a corticosteroid (i.e. claims 6-8) or an atropine-like derivative, such as ipratropium bromide (i.e. claims 9-10).

The primary differences between the claims of the instant application and the claims of copending '075 are that (1) the claims of copending '075 do not recite the limitation that the compositions contain water in an amount of 0-5% w/w or up to 5%; and (2) the independent claim of copending '075 does not specify that one of the two dissolved medicaments is salmeterol. These deficiencies are rendered obvious per the language of the claims of the instant

application because the claims of copending '075 do not indicate that water has been added. Thus, the claims of copending '075 necessarily comprise 0% w/w water and are an obvious variant of the claims of the instant application. Regarding the presence of salmeterol in the formulations administered in the claimed method of copending '075, it is clear that formulations comprising a beta-adrenergonic agonist, such as salmeterol, were contemplated obvious variations, as evidenced by dependent claim 3 of copending '075. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-3, 5, 15, and 18-20 *prima facie* obvious over claims 1, 3, 6-11, and 13 of copending Application No. 12/225,075 (copending '075).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Adjei references (U.S. Patent No. 7,074,388 and US 2003/0091512) are relevant because these teach the stabilization of aerosol medicinal formulations by the addition of water. Neale et al. (U.S. Patent No. 5,695,744) is relevant because it teaches the stabilization of suspension aerosol formulations of particulate beclomethasone dipropionate by the addition of water.

Claims 1-21 are rejected. Claims 5-8, 10, 12-17, and 19 are objected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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